

# **EXHIBIT A170**

## A Prospective Study of Weight Gain after Premenopausal Hysterectomy

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### Abstract

**Purpose:** Many women who have had hysterectomies have the perception that they gained weight after surgery that cannot be attributed to changes in diet or physical activity. The purpose of this analysis was to assess weight gain in premenopausal women in the first year after hysterectomy compared with a control group of women with intact uteri and ovaries.

**Methods:** As part of a prospective cohort study designed to assess the risk for ovarian failure after premenopausal hysterectomy, weight was measured at baseline and 1-year follow-up in 236 women undergoing hysterectomy and 392 control women. Changes in measured weight and reported weight were assessed. Unconditional logistic regression analyses were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for weight gains of >10 pounds.

**Results:** Women with hysterectomies weighed more and had a higher mean body mass index (BMI) than control women at baseline. Mean weight gain was 1.36 kg (~3 pounds) for women with hysterectomies vs. 0.61 kg (~1.3 pounds) for control women ( $p = 0.07$ ). Weight gain of >10 pounds occurred in 23% of women with hysterectomies compared with 15% of control women (multivariable OR = 1.61, 95% CI 1.04 = 2.48).

**Conclusions:** Women undergoing hysterectomies appear to be at higher risk for weight gain in the first year after surgery. Heavier women and women who have had weight fluctuations throughout adulthood may be at greater risk for postsurgical weight gain, suggesting that lifestyle interventions to maintain or lose weight may be particularly helpful for these women in the months following hysterectomy.

### Introduction

H YSTERECTOMY IS THE MOST COMMON nonobstetrical surgical procedure among women, with approximately 600,000 surgeries performed annually in the United States.<sup>1,2</sup> Approximately one third of women will have a hysterectomy during their lifetime, and one quarter of women will have a hysterectomy before menopause.<sup>3</sup> Among premenopausal women, most hysterectomies are performed for benign conditions, with the most frequent indications being leiomyomas, dysfunctional bleeding, endometriosis, and pelvic organ prolapse.<sup>1,2</sup>

The vast majority of women undergoing hysterectomies experience relief of the symptoms that led to the surgery and report a high level of satisfaction with the procedure.<sup>4-8</sup> Although most women are happy with the surgical outcomes,

weight gain is a frequent complaint posthysterectomy.<sup>4</sup> Anecdotal reports from clinicians as well as on-line message boards suggest that many women who have had hysterectomies have the perception they gained weight that cannot be attributed to changes in diet or exercise habits.

Despite the high frequency of hysterectomy, there are few data on the relation between hysterectomy and weight gain. Cross-sectional data indicate that women who have had a hysterectomy without bilateral oophorectomy weigh more, have higher body mass index (BMI), and are more likely to be obese than women with intact uteri and ovaries.<sup>9-11</sup> Postsurgical weight gain has been reported in one prospective follow-up study of women undergoing hysterectomy,<sup>4</sup> but the lack of a control group of women without hysterectomy precludes concluding the weight gain was related to the surgery.

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As part of an ongoing prospective cohort study designed to evaluate the risk for ovarian failure among premenopausal women undergoing hysterectomy without bilateral oophorectomy, we compared weight change among women having hysterectomies in the first year after their surgery with that of a control group of women with intact uteri.

## Materials and Methods

Data were obtained from women enrolled in the Prospective Research on Ovarian Function (PROOF) study, a cohort study designed to evaluate hormonal changes in women undergoing premenopausal hysterectomy for benign conditions. Women undergoing hysterectomy at hospitals in the Durham, North Carolina, area in 2004–2006 were identified through referrals from gynecology practices and review of operating room schedules at the hospitals. Eligible women were aged 30–47 years, undergoing hysterectomy for a non-cancerous condition, and were expected to have at least one ovary remaining after surgery. Potential participants were sent a letter from their physicians describing the study and inviting their participation. The letter was followed by a phone call from a study interviewer who verified eligibility and confirmed that the woman was premenopausal as evidenced by at least one menstrual period in the past 3 months, had no history of cancer (except nonmelanoma skin cancer), and was able to complete an interview in English. If the woman agreed to participate, an appointment was scheduled for an interview and blood draw before her surgery. Most interviews and blood draws were performed in conjunction with the woman's preoperative visit, but some were conducted at the woman's home or another mutually convenient location. The comparison group of women without hysterectomy was recruited using brochures in gynecology and family practice offices and advertisements in publications placed in the clinics and doctors' offices from which the women undergoing hysterectomy were identified. Eligibility requirements were similar to those for the women undergoing hysterectomy, plus they could not be currently pregnant. The study protocol was approved by the Institutional Review Board at Duke University Medical Center.

During the baseline study visit, the interviewer obtained written informed consent, administered a questionnaire approximately 45 minutes in length, drew a blood sample, and took anthropometric measurements (height, weight, and waist and hip circumferences). Height was measured to the nearest centimeter and weight to the nearest kilogram. BMI was calculated as  $\text{kg}/\text{m}^2$ . Study participants were recontacted 1 year later, at which time another serum specimen was obtained, questionnaire information was updated, and anthropometric measurements were performed.

Data obtained with the questionnaire included demographic characteristics, reproductive history (menstrual characteristics, pregnancy history, infertility treatment, contraceptive use), medical and gynecological history, gynecological history of mothers and sisters, menopausal symptoms, and lifestyle characteristics (smoking, alcohol consumption, limited diet history, physical activity). Women were queried about their usual frequency of strenuous and moderate physical activity over the past 2 years, at baseline, and over the past year at follow-up. Strenuous activity was defined as activity that increases one's heart rate or makes one breathe heavily,

such as running or sports at a competitive level. Moderate physical activity was defined as activities, such as brisk walking or sports at a social level. Women also reported trends in their weight during adulthood (weigh less than as a young adult, weight was stable  $\pm 10$  pounds throughout adulthood, weigh more than as a young adult, or weight fluctuates with gains and losses of  $>10$  pounds on two or more occasions) and their perception of how their weight changed in the year between baseline and 1 year follow-up. Women undergoing hysterectomy also signed a consent form allowing access to the medical records related to their surgery to confirm that a hysterectomy without bilateral oophorectomy had been performed and to obtain information on the preoperative and postoperative diagnoses, type of hysterectomy, and pathological diagnoses. Types of hysterectomies were categorized as abdominal (total or supracervical), laparoscopic (complete laparoscopic or laparoscopic-assisted vaginal), or vaginal. Many women had multiple diagnoses (e.g., fibroids, menorrhagia, and pelvic pain) listed on their operative reports. For the purposes of our analyses, the category fibroids includes all women with a diagnosis of fibroids, whether or not other diagnoses were mentioned. The category menorrhagia includes women with menorrhagia or related terminology, such as dysfunctional uterine bleeding or metromenorrhagia, with no mention of fibroids. The Other category includes such conditions as pelvic organ prolapse, stress incontinence, endometriosis, or cervical dysplasia, which were diagnosed in a small number of women and could not be assessed individually.

The current analysis is based on 236 women who underwent hysterectomy and 392 control women who completed their baseline and 1-year follow-up visits and had height and weight measurements from both interview visits. Follow-up rates were 91% among the women with hysterectomies and 95% among the control women. Among the control group, we excluded those who were currently pregnant at follow-up or had delivered in the year between the baseline and follow-up interviews.

## Statistical analysis

Baseline characteristics of the women undergoing hysterectomy and the control women were compared using chi-square tests or Fisher's exact test for categorical variables and Student's *t* tests for continuous variables. Comparisons of changes in weight and BMI between baseline and follow-up were evaluated with analysis of covariance (ANCOVA), controlling for baseline values of these variables. Multiple linear regression was used to estimate change in weight or BMI by hysterectomy status, controlling for baseline characteristics. We also assessed the dichotomous outcome of weight gain  $>10$  pounds, using unconditional logistic regression to calculate odds ratios (ORs) and 95% confidence intervals (CIs) associated with hysterectomy status, controlling for potential confounding variables. Variables evaluated as potential confounders in the multivariable linear and logistic regression models included age, baseline weight, race, marital status, educational level, number of full-term pregnancies, smoking status, current alcohol drinker, physical activity, weight change as an adult, and history of tubal ligation. Terms were included in the model using the categorizations described in Table 1. All analyses were performed with SAS statistical software, version 9.1.3 (Cary, NC).

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TABLE 1. SELECTED CHARACTERISTICS OF WOMEN WITH HYSTERECTOMIES AND CONTROL WOMEN

	<i>Women with hysterectomies (n = 236)</i>		<i>Control women (n = 392)</i>		<i>p value</i>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Age (years) at interview	40.4	4.0	40.3	4.6	0.8
Number of pregnancies	2.6	1.7	2.3	2.0	0.01
Number of full-term pregnancies	1.8	1.3	1.4	1.4	0.002
	<i>n</i>	<i>%</i>	<i>n</i>	<i>%</i>	
Age at interview (years)					0.08
30–34	15	6.4	42	10.7	
35–39	75	31.8	113	28.8	
40–44	106	44.9	151	38.5	
45–47	40	17.0	86	21.9	
Race					0.02
White	113	47.9	231	58.9	
African American	116	49.2	147	37.5	
All other	7	3.0	14	3.6	
Marital status					0.03
Married/living as married	147	62.3	213	54.3	
Single, never married	38	16.1	98	25.0	
Divorced/separated/widowed	51	21.6	81	20.7	
Educational level					<0.0001
Up to high school graduate	152	64.4	174	44.4	
College graduate	61	25.9	117	29.9	
Graduate/professional school	23	9.8	101	25.8	
Number of full-term pregnancies					0.001
None	44	18.6	130	33.2	
One	50	21.2	75	19.1	
Two or three	125	53.0	164	41.8	
Four or more	17	7.2	23	5.9	
History of infertility					0.7
Yes	43	18.2	77	19.6	
No	193	81.8	315	80.4	
Oral contraceptive use					0.4
Ever	218	92.4	354	90.3	
Never	18	7.6	38	9.7	
Tubal ligation					<0.0001
Yes	107	45.3	104	26.5	
No	129	54.7	288	73.5	
Smoking status					0.08
Never smoker	142	60.2	258	65.8	
Former smoker	43	18.2	77	19.6	
Current smoker	51	21.6	57	14.5	
Currently drink alcohol					0.2
No	79	33.5	110	28.1	
Yes	157	66.5	282	71.9	
Strenuous physical activity					<0.0001
Never or <once a month	119	50.4	123	31.4	
Up to 1 time a week	34	14.4	95	24.2	
2–6 times a week	73	30.9	161	41.1	
≥7 times a week	10	4.2	13	3.3	
Moderate physical activity					0.01
Never or <once a month	39	16.5	34	8.7	
Up to 1 time a week	55	23.3	98	25.0	
2–6 times a week	110	46.6	216	55.1	
≥7 times a week	32	13.6	44	11.2	
Physical activity in occupation					0.02
Mainly sitting	94	39.8	198	50.5	
Mainly standing or walking	44	18.6	69	17.6	
Mainly active to very active	67	28.4	74	18.9	
Do not work outside the home	31	13.1	51	13.0	

(continued)

TABLE 1. (CONTINUED)

	<i>Women with hysterectomies</i> (n = 236)		<i>Control women</i> (n = 392)		<i>p value</i>
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>	
Weight pattern during adulthood					0.2
Stable ( $\pm 10$ pounds) or weigh less	67	28.4	130	33.5	
Weigh more now	87	36.9	150	38.7	
Weight fluctuates	82	34.7	108	27.8	
Missing			4		
Change in strenuous physical activity between baseline and follow-up					0.6
Unchanged	135	57.2	211	53.8	
Decreased	56	23.7	107	27.3	
Increased	45	19.1	74	18.9	
Change in moderate physical activity between baseline and follow-up					0.1
Unchanged	100	42.4	192	49.0	
Decreased	53	22.5	90	23.0	
Increased	83	35.2	110	28.1	

## Results

Descriptive characteristics of the women undergoing hysterectomies and the control women are presented in Table 1. The mean age at baseline was approximately 40 years for both groups. Compared with the control group, the women who had hysterectomies were more likely to be African American, be married, have lower educational achievement, have had more pregnancies, and have had a tubal ligation. Women with hysterectomies reported lower levels of both strenuous and moderate physical activity but higher levels of occupational physical activity. They also were somewhat more likely to be current smokers, although the difference was not statistically significant.

In Table 2 we present data on weight and BMI at baseline and follow-up. The mean BMI was quite high for both the women undergoing hysterectomy and the control group (30.8 and 29.2 kg/m<sup>2</sup>, respectively), and more than half of the women with hysterectomies and 38% of the control women would be considered obese (BMI > 30). The women undergoing hysterectomy had statistically significantly higher BMI and weight at both baseline and 1-year follow-up. The mean changes in BMI were 0.51 kg/m<sup>2</sup> and 0.22 kg/m<sup>2</sup> ( $p = 0.06$ ), and the mean changes in weight were 1.36 kg (~3 pounds) and 0.61 kg (~1.3 pounds) ( $p = 0.07$ ) for women with hysterectomies and control women, respectively.

We also examined weight change in pounds and compared reported weight change to measured weight change. Thirty-six percent of women who had hysterectomies had a measured weight gain of >5 pounds compared with 29% of control women. The differences in weight gains between the groups were more prominent when considering larger weight gains, with 23% of women with hysterectomies and 15% of control women having gained >10 pounds. The proportion of women with measured weight loss of >5 pounds was similar in both groups (17%).

Differences between the women undergoing hysterectomy and the control women were larger when based on reported weight change rather than measured weight change

( $p = 0.001$  for reported change vs.  $p = 0.07$  for measured weight change). Both groups of women tended to underestimate weight gain, although the proportion of women who underreported weight gain was smaller among the women having hysterectomies than among the control women (Table 2).

We examined weight gain by categories of baseline BMI to assess whether heavier women were more likely to gain weight (Table 3). Among women with hysterectomies, women with higher baseline BMI had larger increases in weight and BMI, but this pattern was not observed among the control women. When considering categories of weight gain, the proportion of women reporting a >10 pound gain increased with increasing baseline BMI in both the women with hysterectomies and the control women. However, within each BMI category, the proportion of women reporting a weight gain of >10 pounds was larger for women with hysterectomies than for control women.

We performed multivariable linear regression analyses assessing changes in weight and BMI controlling for the possible confounders listed in Table 1. A linear regression model adjusted for age and baseline weight showed that women with hysterectomies gained 0.75 kg (~1.7 pounds) more than the control women ( $p = 0.07$ ), whereas a model fully adjusted for all potential confounders in Table 1 showed a difference in weight gain of 0.89 kg (~2.0 pounds,  $p = 0.04$ ). The corresponding models for BMI change between women undergoing hysterectomy and control women were 0.29 kg/m<sup>2</sup> ( $p = 0.07$ ) and 0.33 kg/m<sup>2</sup> ( $p = 0.04$ ), respectively.

Because the differences between women with hysterectomies and controls appeared to be more prominent for larger weight gains and weight gains of >10 pounds would have more clinical relevance, we used logistic regression analyses to assess the association between hysterectomy status and the dichotomous outcome of measured weight gain >10 pounds (approximately 4.5 kg) when controlling for possible confounders. In unadjusted analyses, women who had a hysterectomy were 1.68 (95% CI 1.12-2.53) times as likely to have a weight gain of >10 pounds as the control women (Table 4).

TABLE 2. WEIGHT AND BODY MASS INDEX (BMI) CHARACTERISTICS COMPARING WOMEN WITH HYSTERECTOMIES AND CONTROL WOMEN

	Women with hysterectomies (n = 236)		Control women (n = 392)		p value
	Mean	SD	Mean	SD	
BMI (kg/m <sup>2</sup> ) at baseline	30.8	(7.1)	29.2	(7.8)	0.008
BMI (kg/m <sup>2</sup> ) at 1 year follow-up	31.3	(7.5)	29.4	(7.8)	0.003
Change in BMI	0.51	(2.2)	0.22	(1.7)	0.06 <sup>a</sup>
Weight (kg) at baseline	82.8	(19.6)	78.7	(20.9)	0.01
Weight (kg) at 1 year follow-up	84.2	(20.8)	79.3	(21.2)	0.005
Change in weight (kg)	1.36	(5.7)	0.61	(4.5)	0.07 <sup>a</sup>
	<i>n</i>	%	<i>n</i>	%	<i>p value</i>
BMI (kg/m <sup>2</sup> ) at baseline					
<18.5	2	(0.9)	4	(1.0)	0.01
≥18.5–<25	59	(25.0)	134	(34.2)	
≥25–<30	54	(22.9)	105	(26.8)	
>30	121	(51.3)	149	(38.0)	
Measured change in weight between baseline and follow-up					
>20 pound gain	15	(6.4)	8	(2.0)	0.07
>10–20 pound gain	40	(17.0)	52	(13.3)	
>5–10 pound gain	31	(13.1)	53	(13.5)	
Stable (±5 pounds)	111	(47.0)	213	(54.3)	
>5–10 pound loss	17	(7.2)	34	(8.7)	
>10–20 pound loss	14	(5.9)	24	(6.1)	
>20 pound loss	8	(3.4)	8	(2.0)	
Reported change in weight between baseline and follow-up					
>20 pound gain	16	(6.8)	11	(2.8)	0.001
>10–20 pound gain	30	(12.7)	29	(7.4)	
>5–10 pound gain	28	(11.9)	48	(12.3)	
Stable (±5 pounds)	112	(47.5)	242	(61.9)	
>5–10 pound loss	17	(7.2)	32	(8.2)	
>10–20 pound loss	20	(8.5)	17	(4.4)	
>20 pound loss	13	(5.5)	12	(3.1)	
Missing			1		

<sup>a</sup>Controlling for baseline BMI or weight.

Other factors statistically significantly associated with weight gain >10 pounds in bivariate analyses were higher baseline weight, African American race, single or divorced marital status, lower educational level, current smoking, no alcohol consumption, and weight gain or weight fluctuations during adulthood. In multivariable analyses including age and all variables that were significantly associated with weight gain in bivariate analysis, hysterectomy remained a statistically significant predictor of weight gain >10 pounds (OR = 1.61, 95% CI 1.04–2.48). It is noteworthy that reported physical activity, whether at baseline or change between baseline and follow-up, was not a statistically significant predictor of weight gain in bivariate analyses, and inclusion of terms for physical activity in the multivariable model had essentially no effect on the OR.

We repeated the analyses excluding women who had been pregnant in the year preceding their baseline interview (5 of the women having hysterectomies and 15 of the controls). Results were very similar, with a multivariable OR of 1.67 (95% CI 1.09–2.56). We also performed analyses using reported weight gain of >10 pounds as the outcome. In multivariable analyses, the association with hysterectomy status was stronger (OR = 2.08, 95% CI 1.24–3.49) than for measured weight gain, whereas associations with potential confounders

showed largely the same pattern as for measured weight gain (data not shown).

Among the women with hysterectomies, we examined weight changes by the type of surgery and the indication for surgery. As shown in Table 5, we compared measured weight and BMI at baseline and follow-up for women who had abdominal, laparoscopic, or vaginal hysterectomies. Mean baseline and follow-up weights and BMIs were highest in women who had abdominal hysterectomies and lowest among those who had laparoscopic hysterectomies, with statistically significant differences between groups in regard to BMI but not weight. There were statistically significant changes in weight and BMI between baseline and follow-up among the women who had abdominal hysterectomies, whereas the changes were not significant for women having either vaginal or laparoscopic surgery.

We also examined weight gain by indications for hysterectomy. Baseline weight and BMI were similar in the women with diagnoses of fibroids or menorrhagia and were somewhat higher than for women with other diagnoses. There were statistically significant weight gains between baseline and follow-up among the women with fibroids or menorrhagia, whereas women with other diagnoses showed a slight weight loss.



TABLE 3. CHANGE IN WEIGHT AND BMI BY BASELINE BMI IN WOMEN WITH HYSTERECTOMIES AND CONTROLS

	Women with hysterectomies (n = 236)						Control women (n = 391)					
	BMI <25 (n = 60)		BMI 25-30 (n = 55)		BMI >30 (n = 121)		BMI <25 (n = 138)		BMI 25-30 (n = 105)		BMI >30 (n = 148)	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Weight change from baseline to 1-year follow-up												
>10 pound gain	6	(10.0)	14	(25.5)	35	(28.9)	11	(8.0)	18	(17.1)	31	(21.0)
>5-10 pound gain	9	(15.0)	5	(9.1)	17	(14.1)	21	(15.2)	12	(11.4)	20	(13.5)
Stable ( $\pm$ 5 pounds)	38	(63.3)	23	(41.8)	50	(41.3)	93	(67.4)	54	(51.4)	66	(44.6)
>5-10 pound loss	5	(8.3)	4	(7.3)	8	(6.6)	10	(7.3)	10	(9.5)	14	(9.5)
>10 pound loss	2	(3.3)	9	(16.4)	11	(9.1)	3	(2.2)	11	(10.5)	17	(11.5)
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Weight change (kg)	1.08	(3.4)	1.11	(5.2)	1.65	(6.8)	0.72	(2.7)	0.70	(4.9)	0.45	(5.6)
BMI change	0.39	(1.3)	0.40	(1.95)	0.62	(2.56)	0.27	(1.0)	0.25	(1.8)	0.16	(2.1)

## Discussion

Our study population of women aged 30–47 years showed differences in risk factors between women undergoing hysterectomy and control women that are consistent with reports from other populations.<sup>12–16</sup> Women undergoing hysterectomy had more pregnancies, were more likely to have had a tubal ligation, and were of lower socioeconomic status as measured by educational level.<sup>12–14</sup> The mean BMI of women undergoing hysterectomy was significantly higher than that of the control women, which is consistent with obesity being a risk factor for uterine fibroids,<sup>15,16</sup> the most common indication for hysterectomy among premenopausal women.

Weight gain was a very common occurrence in our overall study population, with 32% of women having a measured weight gain of >5 pounds and 18% having a weight gain of >10 pounds during the first year of follow-up. Our data show that women who had hysterectomies were at higher risk for weight gain, with nearly one quarter of them having weight gains of >10 pounds. Multivariable analyses showed they were 1.62 times as likely as control women to have a weight gain this large, even when accounting for a number of factors, such as baseline weight, race, marital status, educational level, smoking status, and weight change as an adult, as potential confounders.

Weight gain is a common complaint after hysterectomy, with many women having the perception that weight gain occurred even though they did not change their diet or exercise patterns; therefore, we were interested in comparing perceived weight changes with measured weight changes. Both the control women and the women undergoing hysterectomy tended to underreport weight gain, but underreporting of weight gain was more common among the controls. This may reflect that women who had hysterectomies were more aware of their weight and reported it more accurately, or they were more likely to acknowledge weight gain if they believed there was a plausible reason for it (i.e., their surgery).

To our knowledge, there are no other published reports of prospective studies of weight changes after hysterectomy that included a comparison group of women with intact uteri. Our

results are consistent with a report from the prospective Maine Women's Health Study, which listed weight gain as one adverse outcome of hysterectomy.<sup>4</sup> This study did not quantify weight gain, however, and because it did not include controls, it was not possible to conclude that the observed weight gain was greater than what would be expected in an age-matched group of women. Our data indicate that weight gain, although common in this age range, is more likely to occur in women undergoing hysterectomy.

Because weight was measured only at baseline and after 1 year of follow-up, it was not possible for us to determine the trajectory of weight gain. We could not determine, for example, if the weight gain occurred steadily over the year or if the women having hysterectomies gained weight primarily during the weeks immediately after the surgery, when they were recovering but were restricted in their activities. Our data on weight gain by type of hysterectomy suggested that women with abdominal hysterectomies had larger weight gains than those who had laparoscopic or vaginal hysterectomies. The average recovery period from abdominal hysterectomies is longer than the recovery period for other types of hysterectomies.<sup>17</sup> Thus, our data are consistent with a hypothesis that weight gain may be associated with longer periods of activity limitations. Women with abdominal hysterectomies also weighed more at baseline, suggesting they were predisposed to weight gain independent of the type of hysterectomy they had or the length of recovery.

Analysis of weight gain by indication for hysterectomy showed greater weight gain for women with diagnoses of fibroids or menorrhagia compared with other diagnoses. It is well established that obesity is a risk factor for fibroids,<sup>18</sup> and the greater weight gain we observed among women with fibroids may be a reflection of their higher baseline weight. It is more difficult to speculate on the reasons for differences in the observed weight gain among the women with menorrhagia or other diagnoses. Menorrhagia is not so much a precise diagnosis as a description of a symptom that may be caused by diverse etiologies. Similarly, the Other category includes multiple diagnoses, some of which (e.g., endometriosis) may be inversely associated with weight. It is likely that the observed

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TABLE 4. ODDS RATIOS (ORs) AND 95% CONFIDENCE INTERVALS (CIs) FOR MEASURED WEIGHT GAIN OF &gt;10 POUNDS COMPARING WOMEN WITH HYSTERECTOMIES AND CONTROL WOMEN

Variable	Categories	Bivariate models <sup>a</sup>		Multivariable models <sup>b</sup>	
		OR	(95% CI)	OR	(95% CI)
Hysterectomy status	No	1.00		1.00	
	Yes	1.68	(1.12–2.53)	1.61	(1.04–2.48)
Age at interview (years)	45–47	1.00		1.00	
	40–44	1.39	(0.79–2.43)	1.22	(0.68–2.20)
	35–39	1.36	(0.75–2.47)	1.15	(0.61–2.16)
	30–34	0.91	(0.38–2.22)	1.02	(0.40–2.61)
Baseline weight	Continuous	1.02	(1.01–1.03)	1.01	(1.00–1.02)
Race	White	1.00		1.00	
	African American	1.81	(1.20–2.74)	1.23	(0.76–1.98)
	Other	0.98	(0.28–3.45)	0.94	(0.26–3.46)
Marital status	Married/living as married	1.00		1.00	
	Single	2.15	(1.32–3.50)	1.88	(1.09–3.23)
	Divorced/widowed	1.82	(1.10–3.02)	1.33	(0.78–2.27)
Educational level	≤High school graduate	1.00		1.00	
	College graduate	0.56	(0.34–0.91)	0.74	(0.44–1.26)
	Graduate degree	0.50	(0.28–0.91)	0.72	(0.37–1.38)
Number of full-term pregnancies	0	1.00			
	1	0.86	(0.47–1.58)		
	2–3	0.92	(0.56–1.49)		
	≥4	1.42	(0.63–3.20)		
Smoking status	Nonsmoker	1.00		1.00	
	Former smoker	1.61	(0.97–2.68)	1.83	(1.07–3.13)
	Current smoker	1.85	(1.11–3.10)	1.66	(0.95–2.91)
Current alcohol drinker	No	1.00		1.00	
	Yes	0.61	(0.40–0.92)	0.71	(0.45–1.11)
Strenuous physical activity	Never or < once a month	1.00			
	Up to 1 time a week	0.86	(0.50–1.46)		
	2–6 times a week	0.59	(0.36–0.94)		
	≥7 times a week	0.75	(0.24–2.30)		
Moderate physical activity	Never or < once a month	1.00			
	Up to 1 time a week	0.84	(0.43–1.64)		
	2–6 times a week	0.70	(0.38–1.29)		
	≥7 times a week	0.50	(0.21–1.18)		
Occupational physical activity	Mostly sitting	1.00			
	Mostly standing/walking	1.24	(0.72–2.14)		
	Active	0.99	(0.59–1.68)		
	Not employed	0.95	(0.50–1.82)		
Change in strenuous physical activity (follow-up vs. baseline)	No change	1.00			
	Increased	0.77	(0.44–1.36)		
	Decreased	1.06	(0.66–1.69)		
Change in moderate physical activity (follow-up vs. baseline)	No change	1.00			
	Increased	1.07	(0.67–1.73)		
	Decreased	1.28	(0.78–2.13)		
Weight change as adult	Stable or weigh less	1.00		1.00	
	Gained weight	1.92	(1.11–3.31)	1.17	0.65–2.13
	Weight fluctuates	2.47	(1.42–4.30)	1.67	0.93–3.00
Tubal ligation	Yes	1.00			
	No	0.80	(0.54–1.21)		

<sup>a</sup>Models assessed risk for weight gain >10lbs with each variable individually.<sup>b</sup>Multivariable model contained terms for age and all variables that had statistically significant associations in bivariate analyses.

differences in weight gain for various diagnoses are related to baseline weight, but the inability to look at more precise categorizations of diagnoses other than fibroids makes it difficult to make a firm conclusion about these associations.

Further follow-up of this cohort, which is continuing, will provide insight into the long-term patterns of weight change among women in their 30s and 40s. We will be able to de-

termine if the pattern of greater weight gain among women who had hysterectomies continues or if it is a phenomenon limited to the time shortly after surgery. We also will be able to examine how the weight changes correlate with hormonal changes related to the menopausal transition.

Although our study clearly suggests an association between hysterectomy and weight gain, the limitations of our



TABLE 5. CHANGE IN WEIGHT AND BMI BY TYPE OF HYSTERECTOMY AND DIAGNOSIS

	n	Baseline weight (kg)	Weight at follow-up (kg)	Weight change (kg)	p value <sup>a</sup>	Baseline BMI (kg/m <sup>2</sup> )	BMI at follow-up (kg/m <sup>2</sup> )	BMI change (kg/m <sup>2</sup> )	p value <sup>a</sup>
<b>Hysterectomy type</b>									
Abdominal	110	85.0	86.8	1.8	0.002	32.0	32.7	0.7	0.001
Vaginal	62	82.5	83.7	1.2	0.1	30.2	30.6	0.4	0.2
Laparoscopic	62	79.7	80.6	0.9	0.2	29.4	29.7	0.3	0.2
Missing	2								
p value <sup>b</sup>		0.2	0.2	0.6		0.05	0.03	0.5	
<b>Diagnosis</b>									
Fibroids	156	83.5	85.0	1.5	0.001	31.3	31.9	0.6	0.001
Menorrhagia	54	83.5	85.3	1.8	0.04	30.6	31.2	0.6	0.06
All others	24	77.9	77.7	-0.2	0.9	28.0	28.0	-0.1	0.9
Missing	2								
p value <sup>b</sup>		0.4	0.3	0.4		0.1	0.06	0.4	

<sup>a</sup>p value for change between baseline and follow-up.<sup>b</sup>p value for differences between groups (type of hysterectomy or diagnosis).

data must be acknowledged. The control women for the study were recruited using brochures and advertisements placed in clinics and doctors' offices, and there were significant differences between the controls and the women having hysterectomies in several baseline characteristics. Although the control women were volunteers, they are representative of the population from which the cases arose. The proportion of African Americans in the control group is very similar to the proportion in Durham county, North Carolina, where the hospitals are located (37.5% and 37.8%, respectively).<sup>19</sup> The prevalence of overweight or obesity among the controls (65%) is close to the reported figures from the North Carolina Behavioral Risk Factor Surveillance Study indicating two thirds of adults are overweight or obese. More specifically, among North Carolina women aged 35–44, 49% of white women and 79% of African American women are overweight or obese.<sup>20</sup> The differences in race, weight, and other baseline characteristics that we observed are consistent with risk factors for hysterectomy reported in other studies.<sup>12–16</sup> Specifically, the women having hysterectomies had more pregnancies and a lower educational level, were more likely to have had a tubal ligation, and had higher average BMI. The differences in baseline BMI may be of most concern in a study evaluating weight gain. However, because the prevalence of overweight or obesity among the control women is very similar to reported prevalence figures for North Carolina and the United States,<sup>21,22</sup> it is unlikely that the control group represented a group of women who were particularly health and weight conscious. Furthermore, statistical adjustment for differences in baseline characteristics had minimal effect on the ORs for weight gain associated with hysterectomy.

Another possible limitation is that the dietary information collected in the questionnaire was limited, making it impossible for us to assess the extent to which weight gain was due to increased energy intake. The diet questions assessed intake of general categories of food, such as red meat, poultry, fish, vegetables, fruit, and fruit juices, but in insufficient detail to quantify total energy intake, which would be the most relevant measure in regard to weight gain. We found no statis-

tically significant differences between the women undergoing hysterectomies and the controls in intake of these food categories, with the exception of significantly higher fruit intake among controls and significantly higher fruit juice intake among women with hysterectomies. These dietary factors were not significantly associated with weight gain. Based on the similarity of the dietary data between the women with hysterectomies and the controls as well as the known limitations of data obtained from food frequency questionnaires,<sup>23</sup> we do not believe that our results would have been markedly changed if we had more extensive dietary information.

Our study also had the limitation of its observational design, which meant that physical activity was based on self-report. The point estimates associated with high levels of moderate physical activity and increases in moderate or strenuous physical activity between baseline and follow-up were suggestive that physically active women may be at lower risk for weight gain, but these findings were not statistically significant. This could reflect either the moderate sample size of this study or an attenuation of the true effects because of misclassification inherent in self-reported data such as these.

The weight distribution we saw in our population of women in their middle to late reproductive years is consistent with the high reported prevalence of obesity in the United States,<sup>21,22</sup> with a markedly higher prevalence among the women who had hysterectomies. The weight gain we observed is also in line with other follow-up studies of women during midlife, which reported average weight gains of 1.2 pounds (~0.54 kg) over 12 months in one report<sup>24</sup> and 2.25 kg (~5 pounds) over 3 years in another report.<sup>25</sup> The high proportion of obese women and the high proportion of women reporting weight gains of >10 pounds in a single year raise serious concerns about the health of this population. The medical consequences associated with obesity and weight gain are myriad and include higher risks for overall mortality, cardiovascular disease, diabetes, osteoarthritis, certain forms of cancer, and depression.<sup>26,27</sup> In addition, weight gain is associated with lower physical functioning and health-

related quality of life.<sup>28,29</sup> Our data suggest that women undergoing hysterectomy may be at particular risk for these outcomes.

Hysterectomy is performed most commonly on women in their 40s as they are approaching the menopausal transition, a point in life when weight gain is very common. Thus, the constellation of age, hormonal changes, and surgery may be interrelated and contribute to challenges in weight management. Our data showing that women undergoing hysterectomy are at considerably higher risk for large weight gains suggest that it would be very appropriate to target them for lifestyle interventions designed to prevent weight gain. Women who are overweight or obese at the time of surgery or those who have struggled with weight throughout their life, as evidenced by weight fluctuations throughout adulthood, may benefit especially from efforts designed to help them lose weight or prevent further weight gain.

### Conclusions

Data from this prospective cohort study suggest that premenopausal women undergoing hysterectomy without bilateral oophorectomy are at increased risk for weight gain compared with women of similar age with intact uteri and ovaries. Women who are heavier or have had weight fluctuations throughout their life appear to be most at risk and may benefit from lifestyle interventions to prevent weight gain after surgery.

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The authors have no conflicts of interest to report.

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